The prior art discloses the use of various routes of administration to deliver TNF antagonists to the systemic circulation, thereby achieving a therapeutic response.

The novel routes of administration claimed in this application are all routes of anatomically localized administration, including perilesional and intralesional routes. These routes are different than the routes designed for systemic administration, in many important ways.

First, localized anatomic administration (LAA) produces a higher concentration of the drug at the site of pathology. Systemic administration causes the drug to be diluted; LAA bathes the site of pathology in a high concentration of the unmodified drug. This factor alone produces a more substantial therapeutic effect. In fact, there will be clinical circumstances when the therapeutic effect requires high concentrations of drug; in these circumstances systemic administration will be completely ineffective, but LAA will be effective. This is a concentration effect.

Second, LAA allows the unmodified drug to reach the site of pathology. This is critical, because systemic administration allows the drug to pass through the hepatic circulation. The liver is well known to function as a site of drug metabolism. Enzymes in the liver modify drugs, through the cytochrome P450 and other enzyme systems. These modifications can alter the structure and/or function of the drug.

Therefore the novel routes of LAA of consideration in this application, including the intralesional and perilesional routes of administration and drug delivery, are distinguishable from the prior art.

Burt Patent

The Burt Patent, entitled "Imidazole Derivatives as Protective Agents in Reperfusion Injury and Severe Inflammatory Responses" covers the use of Imidazole Derivatives and directly related compounds, alone or in combination for the treatment of certain clinical disorders. The cytokine antagonists claimed in this application are not imidazole derivatives, and have no structural relation to imidazole derivatives. The structure and function of the cytokine antagonists claimed in this application are completely distinct from the imidazole and related compounds of consideration in the Burt patent.

Alexander Patent

The Alexander patent 6,180,355 is entitled "Method for diagnosing and treating chronic pelvic pain syndrome."

Alexander concerns the diagnosis and treatment of chronic prostatitis/chronic pelvic pain syndrome, abbreviated CPPS by the author. "CPPS is the third of four subgroups of prostatitis recognized by the NIH," as stated in the patent.

The claims in this patent are limited to:

"A method for diagnosing chronic pelvic pain syndrome or non-bacterial prostatitis. . ." or "A method for diagnosing a condition in a subject, wherein said condition is associated with elevated levels of GM-CSF." There is a brief mention within the body of the patent of the use of etanercept and other anti-tnf agents.

No claim is made in the present application regarding the use of TNF antagonists for the treatment of chronic prostatitis, non-bacterial prostatitis, or any related conditions.

It is well-known that TNF antagonists are useful for treating certain diseases which are unrelated to the neurological disorders claimed in the present application. Etanercept is FDA approved for the treatment of rheumatoid arthritis; however this does not mean that it is obvious that it can be used for disorders of other organ systems. Although Alexander claims the use of etanercept for the treatment of conditions of the prostate in men, Alexander does not disclose and does not make it obvious that etanercept can be used to treat hearing loss.

Additionally, the novel methods of treatment and routes of administration disclosed in the present application are not disclosed in the Alexander patent.

Claims 1 to 43 were rejected for double patenting in view of U.S. Patent No. 6,177,077. Enclosed is a Terminal Disclaimer to overcome this rejection.

Claims 1 to 43 were rejected for double patenting in view of U.S. Patent No. 6,015,557. Enclosed is a Terminal Disclaimer to overcome this rejection.

Claims 1 to 43 were provisionally rejected for double patenting in view of the Application S.N. 09/654,996. Enclosed is a Terminal Disclaimer to overcome this provisional rejection.

For these reasons, the claims of the present application are patentable.

Respectfully submitted,
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